Neurosurgical Review (2021) 44:1665–1673
https://doi.org/10.1007/s10143-020-01363-7

ORIGINAL ARTICLE

Clinical characteristics and surgical outcomes of ependymomas in the upper cervical spinal cord: a single-center experience of 155 consecutive patients

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Received: 19 May 2020 / Revised: 8 July 2020 / Accepted: 28 July 2020 / Published online: 7 August 2020

Abstract

Ependymomas occurring in the upper cervical spinal cord (above the level of the C4 segment) are rare entities with great therapeutic challenges. This study was aimed to investigate the clinicoradiological characteristics and the prognosis in a large cohort of upper cervical ependymomas from a single institution. This retrospective study enrolled 155 patients with primary ependymomas in the upper cervical spinal cord. The pre- and post-operative clinical and magnetic resonance imaging profiles were collected. The neurological outcomes and survival events were evaluated, and potential independent risk factors were analyzed. There were 82 females and 73 males, with an average age of 43.1 ± 11.3 years. Immediately post-operatively, 118 (76.1%) patients experienced neurological deterioration and 32 (20.7%) patients remained unchanged. Three months after surgery, 61 (39.4%) patients showed deteriorated neurological functions compared to the pre-operative baseline levels. After an average follow-up period of 56.0 ± 24.7 months, the neurological functions were worse than the baseline status in 37 (23.9%) patients and improved in 33 (21.3%) patients, respectively. Logistic regression analysis identified that lower age (≤ 42 years) and lower pre-operative MMS (I–II) were independent protective factors for predicting favorable neurological functions. Multivariate Cox regression analysis revealed that incomplete resection was the only independent risk factor associated with a shorter progression-free survival. Age and pre-operative functional status affect the long-term neurological outcomes, and incomplete resection was associated with a shorter survival. Our findings indicate that gross total resection should be the goal of surgical treatment of upper cervical ependymomas.

Keywords Ependymoma · Upper cervical spinal cord · Intramedullary tumor · Surgical resection · Prognosis

Introduction

Intramedullary spinal cord tumors represent a distinct subset of parenchymal neoplasms in the central nervous system [1]. Ependymoma, arising from the ependymal cells lining the central canal of the spinal cord, is the most common histopathological variant [18]. Although the mechanisms underlying the tumorigenesis of ependymoma remain unclear, spinal ependymoma is generally considered to be a relatively benign entity as anaplastic and malignant metastasis are rarely observed [16]. Clinical manifestations of intramedullary ependymoma are nonspecific and variable based on the region of the spinal cord involved, including localized pain, sensorimotor deficits, myelopathy, proprioceptive dysfunctions, and sphincter dysfunction [3]. Noteworthily, the clinical course may be occult when the ependymoma is located in the mobile spinal segments (thoracic or lumbar) or when the tumor grows slowly; nevertheless, some aggressive ependymomas progress rapidly as white matter fiber tracts in the spinal cord are sensitive to compressive injuries.

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Ependymomas occurring in the upper cervical spinal cord (above the level of the C4 segment) are rare but exceedingly hazardous entities, which may lead to respiratory disturbances or paraplegia [11, 21, 22]. Surgical treatment is the only standard management modality for spinal ependymoma. However, even though remarkable progress has been achieved in microneurosurgery and intraoperative electrophysiological monitoring techniques, surgical resection of upper cervical ependymomas remain extremely challenging for the following reasons: (1) the upper cervical spinal cord is the continuation of the medulla oblongata and has specific anatomical features; (2) ependymomas are not encapsulated and usually poorly demarcated; (3) ependymomas are usually located centrally within the spinal cord, and in less common situations, they may asymmetrically grow into one hemicord; and (4) ependymomas have a rich blood supply from the branches of the anterior spinal artery that penetrate into the spinal cord through the ventral median raphe.

Till now, the clinical characteristics and surgical outcomes of ependymomas in the upper cervical spinal cord have been sparsely reported. In this study, we analyzed the clinical and radiological profiles as well as the prognosis in a large cohort of upper cervical ependymomas from a single institution.

Materials and methods

Patients

This retrospective study enrolled 155 patients with primary ependymomas in the upper cervical spinal cord (involving C1 ~ C4) between January 2012 and September 2019. Ependymoma was diagnosed based on histopathological evidence. The exclusion criteria were the following: (1) patients with lesions originating from the intracranial space and expanding into the spinal canal; (2) pathological diagnosis of subependymoma; (3) incomplete clinical or radiological data; (4) concomitant occipito-cervical deformity; or (5) loss to follow-up.

The study was approved by the Institutional Review Board and Ethics Committee of Beijing Tiantan Hospital.

Demographic and clinical profiles

Demographic and clinical data were collected, including age at surgery, gender, onset of symptoms, and duration of symptoms. The patients' neurological functions were evaluated according to the modified McCormick scale (MMS) [25].

Radiological assessments

Pre-operative magnetic resonance imaging (MRI) with gadolinium-contrast enhancement was available in all patients. The radiological characteristics of ependymomas were evaluated, including tumor location, syringomyelia, intratumoral hemorrhage, and tumor demarcation. Additionally, tumor-to-cord ratio (TCR; Fig. 1a–b) was measured on the contrast axial T1-weighted imaging using the previously described formula: TCR = the largest anteroposterior width of the tumor/the largest cord width at the tumor site [15].

Surgical treatment and pathological evaluation

Surgical resection was performed via a posterior midline approach with the assistance of intraoperative neuroelectrophysiological monitoring. After reviewing the operative logs and post-operative MRI, the extent of surgical resection was determined. Gross total resection (GTR) was defined as tumor removal with surgical margins that were grossly free of tumor cells (~ 100% resection by volume); subtotal resection (STR) was defined as removal of the majority of the tumor (≥ 90% resection by volume); and partial resection (PR) was defined as removal of sectional tumor parenchyma for decompression (< 90% resection by volume). The post-operative radiation treatment or chemotherapy was documented and analyzed. The pathological grade of tumor was evaluated according to the World Health Organization (WHO) classification criteria [12].

Prognostic assessment

The post-operative courses were reviewed, and operation-related and short-term complications were evaluated. Follow-up data for all patients were obtained during individual office visits or telephone interviews. Neurological functions were assessed immediately post-operatively, 3 months after surgery and at the last follow-up.

Statistical analysis

Statistical analyses were performed using IBM SPSS software (version 25.0; Armonk, NY). Continuous variables were presented as "mean ± standard deviation (SD)," and categorical values were expressed as percentages. Univariate statistical analysis (Chi-squared test or continuity correction test) was used to screen the potential risk factors, including age at surgery (≤ 42 years or > 42 years), duration of symptoms (≤ 18 months or > 18 months), levels of spinal cord involvement (≤ 3 levels or > 3 levels), TCR (≥ 0.9 or < 0.9), syringomyelia (present or absent), intratumoral hemorrhage (present or absent), and tumor demarcation (well-defined, or ill-defined), extent of resection (GTR or STR/PR), radiotherapy (present or absent), and pre-operative MMS (≤ II or ≥ III). Additionally, progression-free survival (PFS) was evaluated using the Kaplan–Meier analysis, and results were compared

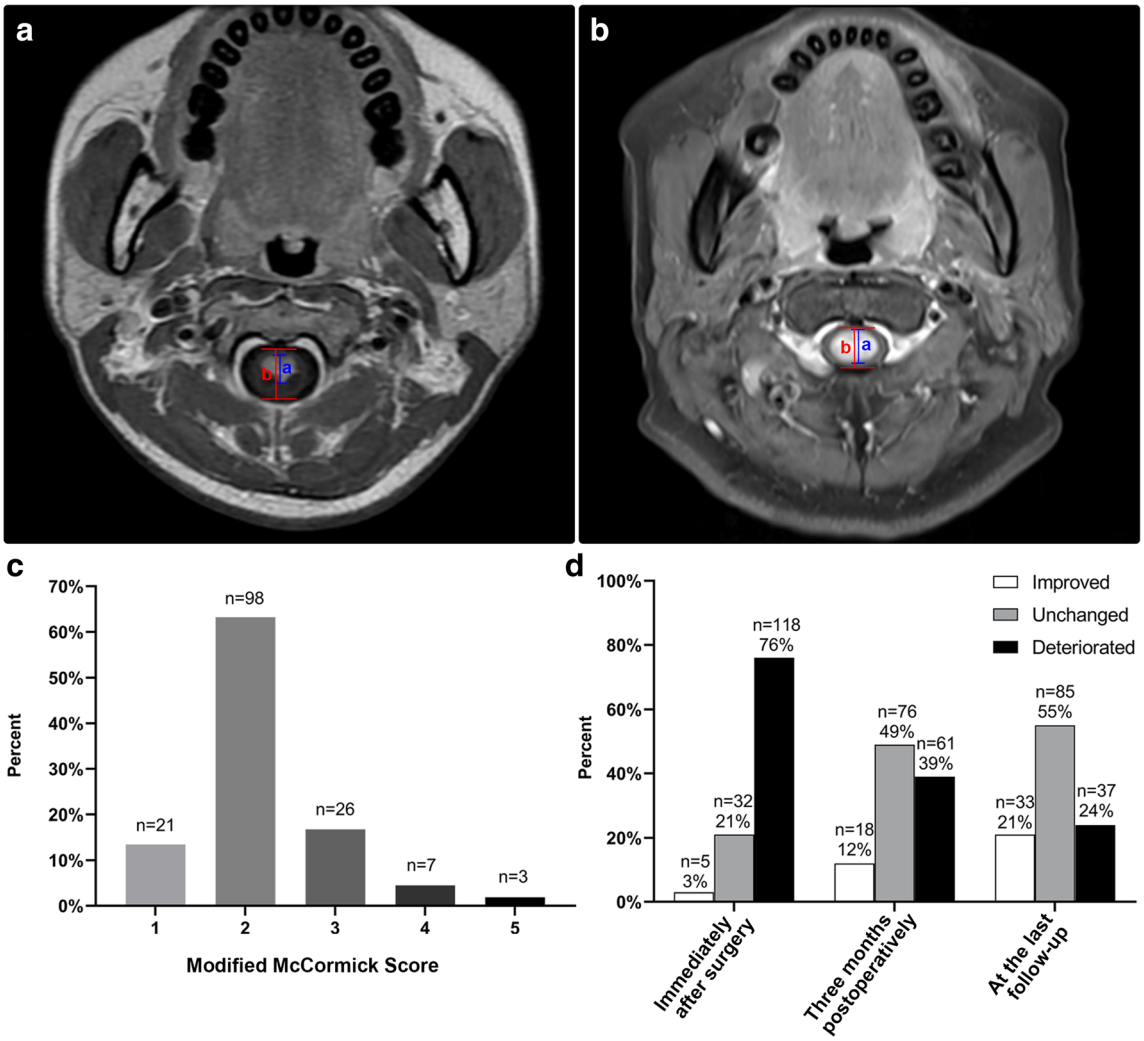

Fig. 1 Representative cases showing the tumor-to-cord ratio (TCR) and statistics of neurological functions. **a** A representative case with a lower TCR (< 0.9; TCR = *a*/*b*; *a* indicates the transverse width of the tumor, and *b* indicates the transverse width of the spinal cord). **b** A representative case with a higher TCR (> 0.9; TCR = *a*/*b*; *a* indicates the transverse width of the tumor, and *b* indicates the transverse width of the spinal cord). **c** Pre-operative neurological functions in patients with upper cervical ependymomas. **d** Post-operative and follow-up neurological outcomes

using the log-rank test. Logistic and multivariate Cox regression analyses were performed to identify the risk factors for clinical outcomes. All the analyses were two-sided and the statistically significant level was set at 0.05.

Results

Clinical manifestations

There were 82 females and 73 males, with an average age of 43.1 ± 11.3 years (range, 20–69 years). The average duration of symptoms from the onset to operation was 22.3 ± 23.2 months (range, 1–120 months). The onset symptoms included localized pain (84/155 cases; 54.2%), dysesthesia/paresthesia (131/155; 85.8%), weakness with or without amyotrophy (89/155; 57.4%), gait abnormality (28/155; 18.1%), sphincter disturbances (22/155; 14.2%), lower cranial nerve dysfunctions (5/155; 3.2%), and dyspnea (3/155; 1.9%). Pre-operatively, 119 patients (76.8%) had mild neurological deficits (MMS I ~ II), 26 patients (16.8%) had moderate neurological deficits (MMS III), and ten patients (6.5%) had severe neurological dysfunctions (MMS IV ~ V). The clinical characteristics were presented in Table 1.

MRI characteristics and treatment

Based on pre-operative spinal MRI, the tumor involved less than three spinal levels in 108 (69.7%) cases. The TCR was ≥ 0.9 in 70 (45.2%) cases and < 0.7 in 14 (9.0%) cases. Syringomyelia and intratumoral hemorrhage were observed in 109 (70.3%) and 48 (31.0%) patients, respectively.

Table 1 Clinical characteristics of 155 patients with upper-cervical ependymoma

Characteristic	No. (%) or mean ± SD	Characteristic	No. (%) or mean ± SD
Gender		Onset symptoms	
Male	73 (47.1%)	Pain	84 (54.2%)
Female	82 (52.9%)	Sensory disturbances	131 (84.5%)
Age (years)	43.1 ± 11.3	Motor dysfunctions	89 (57.4%)
Duration of symptoms (months)	22.3 ± 23.2	Gait abnormalities	28 (18.1%)
Tumor-to-cord ratio		Sphincter disturbances	22 (14.2%)
≥ 0.9	70 (45.2%)	Dysphagia or choking	5 (3.2%)
0.8 ~ 09	44 (28.4%)	Dyspnea	3 (1.9%)
0.7 ~ 0.8	27 (17.4%)	Pre-operative MMS	
< 0.7	14 (9.0%)	I–II	119 (76.8%)
Levels of spinal cord involvement		III	26 (16.8%)
≤ 3	108 (69.7%)	IV–V	10 (6.5%)
3–8	47 (30.3%)	Adjuvant radiotherapy	21 (13.5%)
Syringomyelia	109 (70.3%)	Adjuvant chemotherapy	2 (1.3%)
Intratumoral hemorrhage	48 (31.0%)	Extent of resection	
Tumor border		GTR	115 (74.2%)
Ill-defined	61 (39.4%)	STR	36 (23.2%)
Well-defined	94 (60.6%)	PR	4 (2.6%)
Pathological classification		Post-operative dyspnea	6 (3.9%)
WHO grade II	150 (96.8%)	Follow-up period (months)	56.0 ± 24.7
WHO grade III	5 (3.2%)	Progression or recurrence	13 (8.4%)

MMS modified McCormick scale, *GTR* gross total resection, *STR* subtotal resection, *PR* partial resection

Intraoperatively, the ependymoma was well-defined in 94 (60.6%) cases but poorly demarcated in 61 (39.4%) cases. GTR was achieved in 115 (74.2%) patients, STR in 36 (23.2%) patients, and PR in four (2.6%) patients. Post-operative pathological examinations showed WHO grade II ependymoma in 150 (96.8%) cases and grade III anaplastic ependymoma in only five (3.2%) cases. A total of 21 patients underwent adjuvant radiotherapy and two patients received chemotherapy (temozolomide).

Post-operative courses and neurological outcomes

Post-operative and short-term complications were summarized in Table 2. Kyphosis occurred in 10 (6.5%) patients, and paralysis of lower cranial nerves were noted in 7 (4.5%) patients. Six patients developed dyspnea; the detailed clinical profiles were presented in Table 3.

Immediately post-operatively, 118 (76.1%) patients experienced neurological deterioration, and 32 (20.7%) patients remained unchanged. Three months after surgery, 61 (39.4%) patients showed deteriorated neurological functions compared to the pre-operative baseline levels. After an average follow-up period of 56.0 ± 24.7 months, the neurological functions were improved in 33 (21.3%) patients, unchanged in 85 (54.8%) patients, and worse in 37 (23.9%) patients than the baseline status, respectively. The neurological evaluation results were summarized in Table 4 and Fig. 1c–d. During the follow-up period, 13 (8.4%) patients experienced tumor progression or recurrence, two patients who underwent STR and one patient who underwent PR received a reoperation.

Table 2 Post-operative and short-term complications

Complication	No. (%)
Pulmonary infection	12 (7.7%)
Kyphosis	10 (6.5%)
Wound infection	7 (4.5%)
Dysphagia or choking	7 (4.5%)
Central nervous system infection	6 (3.9)
Respiratory disorder	6 (3.9%)
Cerebrospinal fluid fistula	3 (1.9%)
Deep vein thrombosis	2 (1.3%)
Acute psychosis	2 (1.3%)
Urinary tract infection	1 (0.6)
Hydrocephalus	1 (0.6)

Table 3 Details of cases with post-operative dyspnea

No.	Age (years)	Gender	Tumor Location	TCR	Extent of Resection	Respiratory Disorder			MMS		FU time (months)	Outcome
						Pre-op	Post-op	Tracheotomy	Pre-op	FU		
1	51	Male	C1–C2	≥ 0.9	STR	Yes	Yes	No	IV	III	89	Improved
2	36	Male	Medulla-C4	≥ 0.9	GTR	Yes	Yes	Yes	V	V	12	Unchanged
3	57	Male	Medulla-C4	≥ 0.9	GTR	Yes	Yes	Yes	III	V	39	Deteriorated
4	51	Male	C1–C4	≥ 0.9	GTR	No	Yes	Yes	IV	V	62	Dead
5	28	Male	C2–C4	≥ 0.9	GTR	Yes	Yes	No	III	III	73	Unchanged
6	64	Male	C2–C5	≥ 0.9	GTR	No	Yes	Yes	III	V	15	Deteriorated

TCR tumor-to-cord ratio on the transverse width, *GTR* gross total resection, *STR* subtotal resection, *MMS* modified McCormick scale, *Pre-op* pre-operative, *Post-op* post-operative, *FU* follow-up

Prognostic risk factors

Univariate analysis showed that age, TCR, intratumoral hemorrhage, tumor demarcation, extent of resection, and pre-operative MMS were potential factors affecting the long-term functional outcomes (all $P < 0.05$; Table 5). Logistic regression analysis identified that lower age (≤ 42 years) [$P = 0.022$; odds ratio (OR) = 0.364; 95% confidence interval (CI), 0.153–0.866] and lower pre-operative MMS (I–II) ($P < 0.001$; OR = 0.056; 95% CI, 0.017–0.178) were independent protective factors for predicting favorable neurological functions (Table 6).

Log-rank tests revealed that tumor demarcation, extent of resection, and adjuvant radiotherapy were potential factors affecting the PFS (all $P < 0.05$; Table 7; Fig. 2). Multivariate Cox regression analysis identified that incomplete resection (STR or PR) ($P = 0.003$; OR = 16.934; 95% CI, 2.601–110.235) was the only independent risk factor associated with a shorter PFS (Table 8).

Table 4 Pre-operative, immediately post-operative, and long-term neurological functions

Status	Modified McCormick Score					Total (%)
	I	II	III	IV	V	
Pre-operative	21	98	26	7	3	155
Immediately post-operative						
Improved	0	1	2	0	2	5 (3.2%)
Unchanged	0	24	7	0	1	32 (20.7%)
Deteriorated	21	73	17	7	0	118 (76.1%)
Three months after surgery						
Improved	0	7	7	2	2	18 (11.6%)
Unchanged	4	56	14	1	1	76 (49.0%)
Deteriorated	17	35	5	4	0	61 (39.4%)
At the last follow-up						
Improved	0	23	3	5	2	33 (21.3%)
Unchanged	9	55	19	1	1	85 (54.8%)
Deteriorated	12	20	4	1	0	37 (23.9%)

Discussion

The clinical symptoms of spinal tumors are localization-related. Anatomically, upper cervical spinal cord tumors can be classified into three subgroups: epidural, intradural-extramedullary, and intramedullary. The epidural variants usually show a dumbbell-shaped morphology and are clinically insidious. Previous studies have indicated that occipital and posterior neck pain is the most common onset symptom in patients with intradural-extramedullary upper cervical spinal cord tumors, and some scholars speculated that the neck pain may be caused by the traction or compression forces on the nerve root during neck motion [22]. Additionally, local pain can also be seen in patients with intramedullary tumors, which is thought to be caused by stretching of the dorsal rootlet by the intramedullary tumor [20]. In our series, the most common onset symptoms were sensation disturbances (dysesthesia/paresthesia) and motor dysfunctions. Some authors proposed that glove-like distributed numbness in patients with upper cervical intramedullary tumors represents the typical long-tract sign induced by compression of the dorsal column [19]; nevertheless, some scholars hypothesized that numbness may be caused by secondary vascular insufficiency of the dorsal column nucleus [26].

As ependymomas are the most common spinal intramedullary tumors, there have been abundant clinical studies on these entities. Maximal safe resection is the gold standard for the treatment of spinal ependymomas. As early as 1998, Brotchi and colleagues reported their experience of treating 93 spinal cord ependymomas in which complete resection was achieved in 86 cases; three patients (3.2%) succumbed to post-operative complications, and neurological functions were improved in only

Table 5 Univariate analysis for identifying potential risk factors predicting long-term neurological functions

Factor		MMS at the last follow-up		Chi-square value	*P* value
		I–II	III–V		
Age	≤ 42 years	58 (79.45%)	15 (20.55%)	9.541	**0.002****
	> 42 years	46 (56.1%)	36 (43.9%)		
Duration of symptom	< 18 months	60 (70.59%)	25 (29.41%)	1.039	0.308
	≥ 18 months	44 (62.86%)	26 (37.14%)		
Levels of spinal cord involvement	≤ 3	75 (69.44%)	33 (30.56%)	0.889	0.346
	> 3	29 (61.7%)	18 (38.3%)		
TCR	≥ 0.9	38 (54.29%)	32 (45.71%)	9.489	**0.002****
	< 0.9	66 (77.65%)	19 (22.35%)		
Syringomyelia	Absent	33 (71.74%)	13 (28.26%)	0.639	0.424
	Present	71 (65.14%)	38 (34.86%)		
Intratumoral hemorrhage	Absent	78 (72.9%)	29 (27.1%)	5.266	**0.022***
	Present	26 (54.17%)	22 (45.83%)		
Tumor demarcation	Well-defined	69 (73.40%)	25 (26.60%)	4.304	**0.038***
	Ill-defined	35 (57.38%)	26 (42.62%)		
Extent of resection	GTR	83 (72.17%)	33 (27.83%)	5.203	**0.023***
	STR/PR	21 (52.50%)	19 (47.50%)		
Adjuvant radiotherapy	Absent	91 (67.91%)	43 (32.09%)	0.297	0.586
	Present	13 (61.9%)	8 (38.1%)		
Pre-operative MMS	I–II	97 (81.51%)	22 (18.49%)	48.230	**< 0.001****
	III–V	7 (19.44%)	29 (80.56%)		

Bold represents statistical significance

MMS modified McCormick score, *TCR* tumor-to-cord ratio on the transverse width, *GTR* gross total resection, *STR* subtotal resection, *PR* partial resection

*$P < 0.05$

**$P < 0.01$

nine (9.7%) patients after an 1-year follow-up [5]. As the majority of patients did not recover from severe pre-operative neurological deficits, the authors recommend aggressive surgical therapy before the patient experiences neurological deterioration [5]. In 2011, Boström et al. noted 25% of 57 patients experienced functional improvement at the last available follow-up, and they proposed that incomplete resection was the only independent predictor of PFS [4]. In 2015, German neurosurgeon Klekamp analyzed the surgical morbidity and long-term outcomes in 100 patients with spinal ependymoma. GTR was achieved in 86.3% of all cases, and 40.1% of patients experienced transient neurological deterioration. After a mean follow-up of 71 months, the neurological functions were improved in 5.9% of patients and remained unchanged in 74.5% of patients. Additionally, the authors

Table 6 Logistic regression analysis for identifying potential risk factors predicting long-term neurological functions

Factor	Odds ratio	95% confidence interval	*P* value
Lower age (≤ 42 years)	0.364	0.153–0.866	**0.022***
Lower TCR (< 0.9)	0.900	0.333–2.436	0.836
No intratumoral hemorrhage	0.492	0.180–1.349	0.168
Well-defined tumor demarcation	0.901	0.291–2.794	0.857
GTR	0.791	0.257–2.434	0.682
Lower pre-operative MMS (I–II)	0.056	0.017–0.178	**< 0.001****

TCR tumor-to-cord ratio on the transverse width, *GTR* gross total resection, *MMS* modified McCormick scale

*$P < 0.05$

**$P < 0.01$

Table 7 Univariate analysis for identifying potential factors associated with progression-free survival

Factor	Chi-square (log-rank) value	*P*
Gender	2.267	0.132
Age	0.171	0.679
Duration of symptoms	1.475	0.225
Levels of spinal cord involvement	0.378	0.539
TCR	2.578	0.108
Syringomyelia	0.137	0.711
Intratumoral hemorrhage	0.002	0.965
WHO pathological grade	1.139	0.286
Tumor demarcation	8.178	**0.004****
Extent of resection	26.010	**< 0.001****
Adjuvant radiotherapy	5.745	**0.017***

TCR tumor-to-cord ratio on the transverse diameter

*$P < 0.05$

**$P < 0.01$

found that the tumor recurrence rate was significantly correlated with the extent of resection (4.2% in patients with GTR vs. 18.5% in patients with PR) [9]. In the present study, 52% of all patients experienced transient neurological deterioration and 21% of patients showed functional improvement at the last follow-up, which were consistent with the results in previous reports. These findings suggest that functional outcomes and survival of upper cervical ependymomas have no remarkable difference with those of spinal ependymomas at other levels.

Post-operative complications following surgical resection of upper cervical ependymomas are variable and usually severe. Nonspecific complications of intramedullary spinal tumors include post-operative hemorrhage, infection, kyphosis, deep vein thrombosis, and cerebrospinal fluid fistula [9]. Additionally, due to the specific location, upper cervical ependymomas may invade surrounding neurovascular structures, such as the craniocervical spinal cord parenchyma, the obex of the medulla oblongata, and posterior cranial nerves. Therefore, patients with upper cervical ependymomas may develop respiratory disorders, lower cranial neuropathy, or even paraplegia. In the current series, six patients (3.9%) experienced dyspnea and seven patients (4.5%) experienced dysphagia or choking post-operatively. Considering the relatively low incidence of these serious complications, surgical resection of upper cervical ependymomas is a safe approach.

The rationality of post-operative radiotherapy in patients with spinal ependymoma remains controversial. Kopelson et al. recommended radiation at doses ranging from 40 to 50 Gy for treating intramedullary spinal ependymomas even following complete surgical resection [10]. Whitaker et al. also found that radiotherapy could lead to long-term tumor control in over half of patients with residual spinal ependymoma [23]. However, more scholars argue that radiotherapy may have no benefit for preventing tumor recurrence [2, 7, 13, 14, 17]. Sun et al. performed a meta-analysis to identify the prognostic factors of intramedullary Grade II ependymomas and they found that radiotherapy was associated with shorter PFS, indicating radiotherapy may be detrimental to survival [17]. A large-scale epidemiological analysis using the Surveillance, Epidemiology, and End Results (SEER) database also revealed consistent results [2]. In our study, we noted that patients who received adjuvant radiotherapy had significantly shorter PFS than those who did not receive adjuvant radiotherapy. The role of radiation in patients with spinal ependymomas needs more clinical evidence.

Till now, studies focusing on the surgical outcomes of upper cervical ependymomas remain sparse. The independent risk factors predicting a poor prognosis are still controversial. Wang et al. investigated the long-term surgical outcomes of upper cervical spinal cord tumors in 51 consecutive cases, and the multivariate regression analyses showed that the level of tumor ($P = 0.044$) and tumor size ($P = 0.045$) were independent risk factors for a poor prognosis [21]. Noteworthily, in this study, although the extent of surgical resection (GTR vs. STR) was associated with prognosis in the univariate analysis ($P < 0.001$), this factor did not yield a statistical significance in the multivariate regression analysis ($P = 0.997$). However, Wostrack et al. performed a multicenter retrospective study involving 158 adult patients with spinal ependymomas, and they found that GTR ($P = 0.037$), WHO grade II ($P = 0.009$), and low Ki-67 index ($P = 0.005$) were independent prognostic factors for PFS [24]. In the present study, the multivariate Cox regression analysis identified incomplete resection (STR or PR) as an independent risk factor predicting a shorter PFS ($P = 0.003$). Additionally, numerous studies have indicated that worse pre-operative functional status was associated with poor outcomes [6, 8]. In our study, logistic regression analysis identified lower age (≤ 42 years) ($P = 0.022$) and lower pre-operative MMS (I–II) ($P < 0.001$) were independent protective factors for predicting favorable neurological functions, which is consistent with previous reports. Peker et al. proposed the term "tumor/cord ratio (TCR)" that provides a quantized parameter for evaluating the transverse width of the tumor; they found that high TCR (> 0.80) was not statistically correlated with pre-operative neurological dysfunctions, while high TCR was significantly associated with poorer outcomes [15]. In the current study, although the univariate analysis identified TCR as a potential risk factor predicting long-term

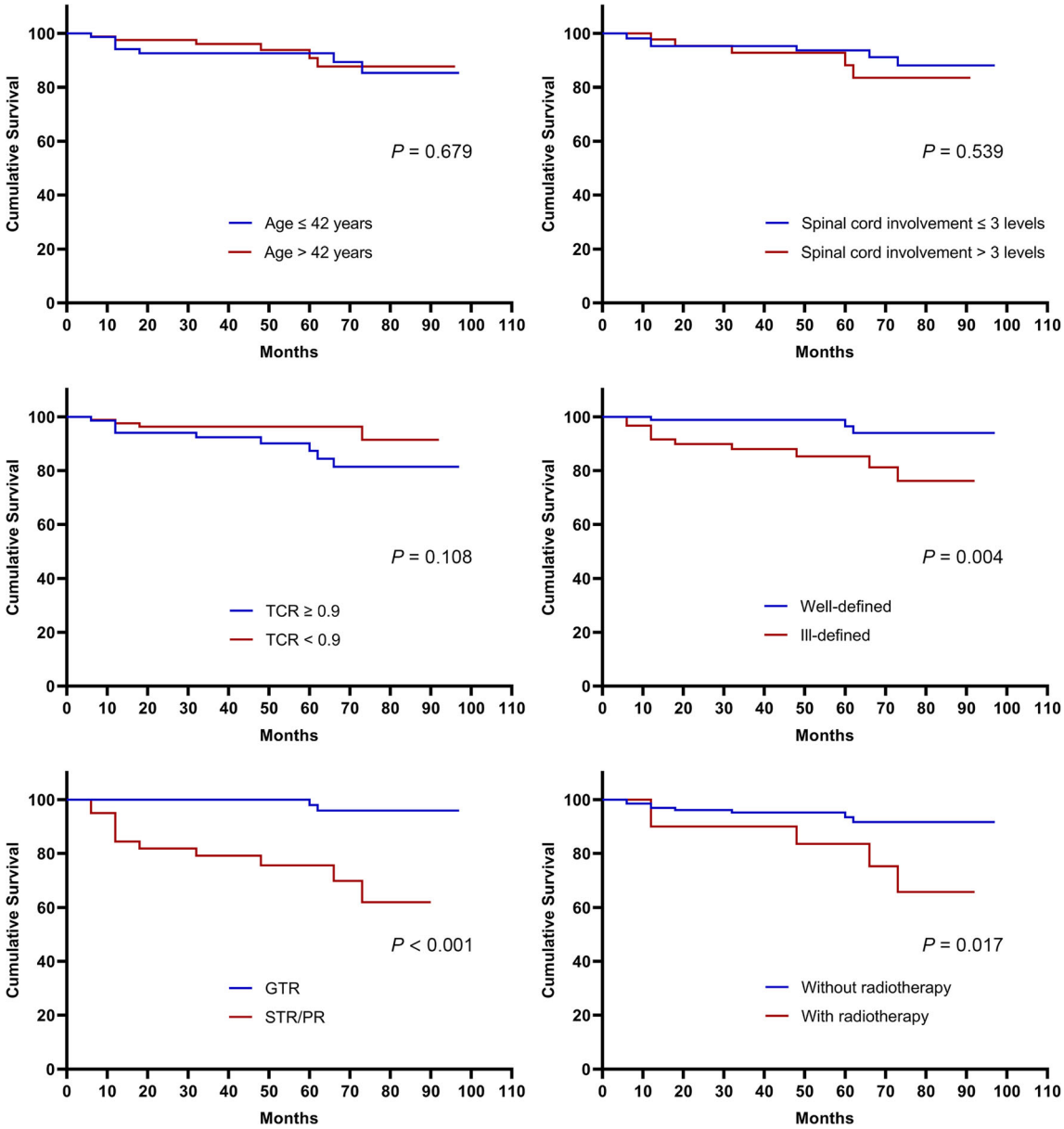

Fig. 2 Results of log-rank tests. Log-rank tests revealed that tumor demarcation, extent of resection, and adjuvant radiotherapy were potential factors affecting the progression-free survival, while age, tumor length, and tumor-to-cord ratio were not significantly correlated with the progression-free survival

neurological functions ($P = 0.002$), further logistic regression analysis showed that TCR was not associated with the functional outcomes ($P = 0.836$). Moreover, no statistical correlation between TCR and progression-free survival was noted.

Conclusions

Upper cervical ependymomas are clinically challenging entities. Age and pre-operative functional status were independent risk factors affecting the long-term neurological outcomes.

Table 8 Multivariate Cox regression analysis for identifying factors associated with progression-free survival

Factor	Odds ratio	95% confidence interval	*P* value
Ill-defined tumor demarcation	0.857	0.175–4.198	0.849
Adjuvant radiotherapy	1.621	0.516–5.094	0.408
Incomplete resection	16.934	2.601–110.235	**0.003****

**$P < 0.01$

Incomplete resection (STR or PR) was an independent risk factor associated with a shorter survival, and therefore, gross total resection should be the goal of surgical treatment of upper cervical ependymomas.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval The work was approved by the Institutional Review Board of Beijing Tiantan Hospital.

Informed consent Informed consent was not sought as a retrospective design was used.

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